

12-16-05

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Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**RE: Application No. 10/620,212, Filing Date 7/15/2003, Office Action 11 /16/05 Examiner Manuel Mandez**

Sir,

Thank you for helping the Applicant respond properly to your recent office action. The applicant now encloses his comments emailed to the Examiner on 12/1/05.

Immediately below is a summary of arguments to overcome objections to §102 and §103 for revised claims 14-31, an elected subset from claims 14 - 43. A more detailed discussion of patentability for all original claims 14 - 43 follows this section.

### **A Summary of Patentability Arguments for Elected Claims 14-31**

#### **§102 – Novelty**

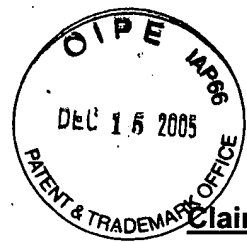
- **Physical Feature:** The feature of **heterogenous and compliant tubing** is not recited in any of references.
- **Operational Feature:** The operation of **high frequency (1-20 Hz) surface pulsations for augmenting heat transfer** is a new use not cited in any of the references.
  - The Applicant agrees that Taheri recites the use of pulsations to “prevent blood from clotting”. However, it does not address the key arterial blood heat transfer challenge – effective heat exchange without constricting the blood flow area. As stated Taheri’s patent, a simple homogenous compliant vessel will lead to a “constricted annular passageway” (Column 5, paragraph 1, Figures 1 and 2).

#### **§103 – Nonobvious**

- These physical and operation features lead to new and unexpected results. Using the heterogenous compliant surfaces with high frequency pulsations leads to substantial increases in heat transfer performance ( Figure 25 of this application is an example).
- These features were recognized by the National Institute of Health as “highly innovative”, rewarding the Applicant with a small business research grant to continue development (July 2005).
- No reference or combination of references taught to combine these features to increase heat transfer and minimize blood flow restriction. None of the references discusses the potential negative impact of the heat transfer process on the blood flow process. The prior art features of uniformly expanding surfaces or corrugated surfaces do not address the unappreciated difficulty of transferring heat in a tiny 4 mm arterial vessel versus a large 25 mm venous vessel. The non-existence of arterial blood coolers supports this claim.

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The Examiner is correct to state (pg. 2 of office action) that clarification is needed. Claim 43 includes an “alignment” claim (step 3 in this Method claim using “distal protection filter”). Yet, Claim 14 does disclose a feature that reduces catheter size: “a plurality of dynamic surface regions” disrupt boundary layers and increase heat exchange, allowing more heat exchange with smaller devices.



## A Detailed Discussion of Patentability Arguments for All Claims 14-43

### Claim Rejections Under 35 U.S.C. 102

The Office Action rejects claims 1 and 5 as being anticipated by U.S. Patent 5,269,758 to Taheri, Office Action, item 1, page 2. Claims 1 and 5 have been rewritten as independent claim 14 and dependent claims 15 through 31 to more precisely define patentability over references cited. Considering these revised claims, the Applicant respectfully traverses this U.S.C § 102 rejection for at least the reason that Taheri fails to disclose all recited features.

The Office Action asserts that Taheri discloses an exchange catheter and a control system to cause an inflatable portion, item 43, to oscillate in the inflated position. The Applicant notes that these novel features as specified and claimed distinguish over Taheri:

1. A non-uniform or heterogeneous compliant heat exchange surface (Figs. 10-18). In general terms, Taheri describes his exchange surface as "inflatable" (Column 1, paragraph 4), and "flexible" (Column 3, paragraph 5). In terms of specific material properties, Taheri states that this feature "resembles a tubular sleeve. This may be formed of a thin walled tubular plastic material, or some other functionally-equivalent material." (Column 3, Paragraph 4). Taheri does not disclose the concept of variable compliant materials.
2. A means for providing for substantial high frequency pressure oscillations in the working fluid (Fig 5, specifically item 10A). Taheri states that "the pump may be operated to circulate heated fluid through the outer and inner chambers. At the same time, the pump may be operated to pressurize said fluid so as to cause the flexible portion to bow outwardly to an inflated position (as shown in Figs. 1 and 2) and may be further caused to pulsate pressure of such fluid to cause flexible wall portion 43 to oscillate, thereby preventing blood from clotting on the flexible portion." (Column 4, paragraph 3). Pumps during typical operation do not create substantial pressure oscillations. Taheri does not sufficiently disclose the means by which pressure oscillations are achieved. As a result, is it impossible for the Applicant to ascertain the magnitude and frequency of the pressure oscillations. Furthermore, it is

important note that the sole purpose of the pressure oscillations as indicated by Taheri is “preventing blood from clotting on the flexible portion” which is in contrast to the primary purpose of our pressure oscillation system. The Applicant submits that different design aims logically require different and unique features.

3. A means to reduce the overall outer diameter of the heat transfer device, using a single-lumen catheter (Figs. 19 and 19A). All of Taheri’s concepts involve multi-lumen catheters. Taheri fails to disclose a feature that enables catheter outer diameter size reduction.
4. A means for aligning the heat transfer device inside a blood vessel to expose all heat transfer surfaces (Fig. 26, item 26). Taheri fails to disclose a means to ensure all heat exchange surfaces are aligned inside a blood vessel.
5. A means for rapidly cooling external fluid through minimal working fluid infusion (Figs. 26, item 25 and 5). Taheri does not disclose a method to infuse working fluid.
6. A means for performing simultaneous heat and mass transfer using gas-permeable membranes, having pores ranging from 0.01 to 0.05 micrometers (Fig. 19). Taheri does not disclose a method to carry simultaneous heat and mass transfer through a single exchange surface.

### **Claim Rejections Under 35 U.S.C. 103**

#### **Initial Comments regarding Office Action Statements**

The Office Action rejects claims 2-4 and 6-13 as being unpatentable over Taheri, in view of Dobak, III et al. (US - 6,096,068 ) , Pham et al., ( US – 6,299,599), and Saab ( US – 5,624,392 ), Office Action, item 2, page 3. The Applicant has rewritten these claims as claims 14-43. The Office Action acknowledges that Taheri does not disclose multiple undulation balloons or balloons having the capability to infuse drugs.

Office Action, page 3, third paragraph, states that “In figure 5, the Dobak Patent shows a balloon located in the distal end of the catheter having multiple undulations.” The Applicant submits that this statement is incorrect. Column 12, paragraph three states “the heat transfer element 14 can be made of metal, and may comprise very high thermally conductive material

such as nickel, thereby facilitating heat transfer.” Throughout the specification numerous arguments are made against flexible low thermal conductivity polymer heat exchange materials. Here are two examples. In column 17, paragraph 4, Dobak et al. states “Saab discloses the use of an inflatable and collapsible balloon catheter formed from an elastomeric material. The elastomeric material is not highly conductive but instead the device relies on the thinning of the elastomeric walls in the inflated configuration to facilitate heat transfer.” In column 17, paragraph 5, Dobak et al. comments on another patent (Ginsberg, US 5,486,208) “The balloon has poor thermal conductivity and relies on surface area in the expanded configuration in order to increase the heat transfer properties of the catheter.” The product based on Dobak et al. US 6,096,068 and others is marketed by InnerCool Therapies, Inc, San Diego, California as “The Celsius Control System”. This product uses metal surfaces to exchange heat, not polymers.

Office Action, page 3, third paragraph, states that “Pham et al., Patent shows in figure 9, a catheter have multiple balloons causing multiple undulations in the outer surface of the balloon.” Numerous patents in addition to Pham et al. call for balloons with multiple undulations in the outer surface, including Gobin et al. (US – 6,126,684), Ginsberg (US – 5,486,208) and Dobak et al. (US – 6,261,312). Multiple undulations whether it is on polymers or metal is neither novel nor non-obvious. The Applicant asserts that what is both novel and non-obvious is the concept of using heterogeneous compliant materials to create dynamic surfaces that augment heat transfer. The Applicant’s specification and the revised claims define the invention more precisely to demonstrate the patentability over the prior art.

Office Action, page 4, fourth paragraph, states “that porous materials in the distal end of a catheter to infuse medications is also a conventional enhancement as evidenced in Saab.” The Applicant wishes to make some distinctions and assert that two ideas in the specification and revised claims 14-31, are novel and nonobvious: 1) the use of gas-soluble working fluids inside hollow fiber membranes with micrometer scaled pores and 2) the use of distal orifices and a working fluid control system to deliver working fluid infusion, not drug infusion – although possible, for initial rapid cooling and gradual return to surface cooling to maximize cooling benefit with

minimal infusion volumes. The Applicant seeks to make clear a distinction between porous membranes vs. distal orifices and infusion vs. diffusion. Porous membranes allow gas diffusion through the pores of the membrane with scales ranging from 0.01 to 0.05 micrometers ( $1$  to  $5 \times 10^{-8}$  meters). The gas is typically oxygen dissolved into a working fluid like perfluoro-carbons, a leading substitute to blood. Distal orifices allow liquid infusion or bulk motion of internal liquids into the external fluid environment. These orifices have dimension ranging from 0.1 to 0.5 millimeters ( $1$  to  $5 \times 10^{-4}$  meters), roughly 10,000 times bigger.

Finally the Office Action states “modifying the catheter disclosed by Taheri with a balloon with multiple undulations and infusion capabilities would have been considered an obvious design choice by a person of ordinary skill in the art.” Office Action, page 4, first paragraph. Arguments against this reason for rejection are submitted below.

## **Claim Rejections Under 35 U.S.C. 103**

### **Overall Response**

The Applicant respectfully traverses the 35 U.S.C. §103 rejections as none of the cited references, neither individually or combined, including Leone et al. (US – 5,885,244) and Leschinsky et al. (US – 6,241,706) disclose all the recited features.

### **Feature by Feature, Claim by Claim Arguments**

On page \_\_\_ of this paper the Applicant has argued against claim objections under 35 U.S.C. §102 for the original claims 1 and 5, now rewritten as independent claim 14 and dependent claims 15,16, 18 through 23. Here the applicant respectfully submits arguments against rejections under 35 U.S.C. §103 on a feature by feature, claim by claim basis.

**Features 1& 2: a non-uniform or heterogeneous compliant heat exchange surface and a means for providing high frequency and substantial working fluid pressure oscillations. (Revised claims 14-31 formerly claims 1,2,4,5, and 6).**

**Reason 1: Heterogeneous compliant heat exchange surfaces used together with a means to provide high frequency and substantial working fluid pressure oscillations lead to new and**

unexpected results. In contrast, to a single compliant surface as shown through the art, (Taheri, Pham et al., and Saab) heterogeneous compliant surfaces create segmented boundary layer disruption, resulting in heat transfer augmentation – without increased risk of vessel occlusion. For example, Taheri states that during normal operation of the disclosed catheter, the catheter will create a “constricted annular passageway” (Column 5, paragraph 1). As described in the Applicant’s application, under sections: “Description of Related Art” and “A Clinical Application Example”, the Applicant asserts that the accepted primary goal in current medical practice for treating ischemic organs is the restoration of sufficient blood flow levels. The reduced blood flow levels that will result from a “constricted annular” passageway will likely create even greater organ damage from ischemia. It should be noted that the Applicant shows, in Fig. 2 of the specification, the negative impact of annulus flow restrictions on flow pressure drop performance. This figure shows that as the annular space is “constricted” pressure drop or fluid resistance continues to increase. Increased pressure drop in many cases reflects increased flow resistance. Pulsations, as described in Taheri, in the inflated position will further “constrict” the annular passageway and increase blood flow resistance. Heterogeneous surfaces, as described in the Applicant specification enable localized boundary layer disruption and subsequent heat transfer augmentation without creating substantial fluid resistance.

In another example, Pham et al. describes the static heat exchange balloon as made of a single material such as urethane, nylon, or PET taking with an outer diameter ranging from 4 to 10 mm (column 4, paragraph 3). This design has uniform or homogenous compliance and is too large to be placed into a feeding artery of an ischemic organ – the primary aim of this invention. Pham et al. appropriately entitled their patent for venous applications “Dual Balloon Central Venous Line Catheter Temperature Control System.” The Applicant asserts that this design is not well suited for arterial implementation where vessel inner diameters range from 4 to 8 mm. Finally, Dobak et al. describes a static metallic exchange surface with multiple undulations to create blood side turbulence. As described in the Applicant’s specification, and in the contrast to dynamic heat exchange surfaces enabled through the use of heterogeneous compliant vessels, the energy

used to drive the blood side turbulence in Dobak et al. is harnessed from the hydraulic energy of the blood stream. It is well known in the heat exchanger industry that mixing undulations, while effective at creating fluid turbulence, are also effective at creating pressure drop – a direct indicator that hydraulic energy has been used. The net effect of this design in small vessels, in particular, is again reduced blood flow through the blood vessel.

**Reason 2:** As indicated in reason 1 above, dynamic heterogeneous compliant surfaces address an unrecognized or at least unappreciated problem of catheter heat transfer in small arteries leading to blood flow restriction. The Applicant asserts that none of the cited references adequately address the fundamental design challenge of cooling blood inside arteries: maximizing heat exchange without significantly reducing blood flow rates. As the Applicant states and references in the specification under “Detailed Description”, most passive enhancement techniques (passive meaning that the heat exchange surfaces are not moving or dynamic) have been well-studied in other fields such as the air conditioning industry. This work has shown that for each percentage increase in heat transfer performance with passive enhancement techniques there is an equal or greater amount of increase in pressure drop. The Applicant asserts that cooling blood rapidly while reducing blood flow is not a medical solution for ischemic organs.

**Reason 3 – 5:** The modification of compliant heat exchange surfaces to use heterogeneous compliance was not suggested in the prior art references (#3) and the advantage of this feature was left unappreciated (#4). In fact if these advantages had been suggested or appreciated, those skilled in the art likely would have implemented it by now (#5). Cooling catheter patents, particularly those involving compliant chambers, have been in place for nearly two decades.

**Reason 6 & 7:** How the heterogeneous compliant materials are used involves a new principle of operation (#6) to solve a different problem (#7). The principle of operation based on the combination of heterogeneous compliant materials and a means to produce high frequency substantial working fluid pressure oscillations has not been described in the prior art references (#6). While Taheri suggested pulsating a working fluid for preventing blood clot formation, it does not suggest nor have the other references suggested using dynamic surfaces to augment heat

transfer (#7). The Applicant asserts that the new principle of operation is logically dedicated by the new design aims and as such the Taheri invention does not address the issues of maximizing heat transfer and minimizing fluid flow resistance.

**Reason 8:** Heterogeneous compliant surfaces solve a long felt and unsolved need to cool the blood inside small arteries (4-8 mm inner diameter). For example, while Dobak et al.'s patent claims repeatedly state the use of the device in an artery, this concept, as described, has not be implemented in this manner nor has any other product to best of the Applicant's knowledge.

**Reason 9:** The concept of heterogeneous compliant and dynamic heat exchange surfaces has received professional recognition from the National Institute of Health. A Small Business and Innovative Research grant (Proposal # 1 R43 NS049933-01 A1) for \$140,000 has been awarded to the Applicant under a proposal entitled: An active mixing catheter for selective organ cooling. Proposal reviewers commented that the project described is "highly innovative" (Page 3, Summary Statement from Review group ZRG1 BDCN-K (10) 12/4/04).

**Reason 10-14 regarding combining references:** The prior art references do not suggest that these features be combined in the manner suggested here (#10). The individual references are complete and function in itself, so there is no reason to use parts from or add or substitute parts to any reference (#11). Again, the underlying problem not appreciated by the prior is the challenge of augmenting heat transfer without detrimentally affecting blood flow. The references teach away from each other (#12). For example, Pham et al. and similar teach towards using surface area to enhance heat transfer. Dobak et al. teaches towards using undulations for turbulence inducing (column 11, paragraph 5). Taheri does not focus on enhancing heat transfer and instead teaches towards flexible or inflatable sections that are pulsated to prevent blood from clotting on the flexible surface. No reference teaches towards combining heterogeneous compliant surfaces with a means to provide high frequency substantial working fluid pressure oscillations. It is impossible to combine the references (#13) for two reasons: 1) a means to provide substantial working fluid pressure oscillations is not described and 2) a heat exchange surface that would be used together with these pressure oscillations is not described. Furthermore, if you were able to apply a means



to provide substantial working fluid pressure oscillations to the flexible designs shown in the cited references, blood vessel occlusion would logically occur as the entire homogenous compliant surface would expand. This is in contrast to what occurs when this same pressure oscillation system is applied to Applicant's heterogeneous compliant design, where segmented sections of the surfaces expand and contract at high frequency. Finally, the Applicant asserts that combining heterogeneous compliant surfaces with a means for substantial pressure pulsations leads to an unobvious synergism not recited in the references (#14). In other words, a heterogeneous compliant exchange surface without a means to provide high frequency substantial working fluid pressure oscillations would not perform well. The same may be said in the reverse order.

**Features 3-5: a compliant connective element, an inflatable distal manifold, and a means for delivering and removing working fluid to and from said inflatable distal manifold (grouped as "shuttle system") (Revised claims 32-37 formerly claims 3 and 7).**

**Reason 1:** The shuttle system leads to new and unexpected results. First, since the working fluid only travels through one pathway the shuttle system allows the use of a single-lumen device to achieve blood cooling inside small arteries. Single lumen devices naturally can be made smaller than the multi-lumen devices. This results in substantially less blood flow restriction and substantially smaller artery penetration diameters. None of the cited references apply single lumen devices or suggest concepts similar to the shuttle system. Second, the use of the single lumen design enables the use of a greater quantity of heat exchange tubes at each manifold, see Fig. 19A in Applicant's specification. If a dual lumen, complete circuit design is used, the inner tubes of Fig. 19A can not be installed, as space is required to pass the 2<sup>nd</sup> of two lumens to complete the working fluid circuit. Third, the cyclical motion of coolant also called shuttling of coolant to and from inflatable distal manifold creates heat exchange surface motion, both radially and along the longitudinal axis, to disrupt external fluid boundary layers, augmenting heat transfer rates.

**Reason 2:** As indicated in reason 1 above, the shuttle system addresses an unrecognized or at least unappreciated problem of creating a blood flow restriction when attempting catheter heat

transfer in small arteries. As the references suggest the amount of heat transfer achieved is largely dependent on the amount heat transfer surface and the amount of mixing that happens near that surface. These same references, however, do not solve the problem of enhancing heat transfer while minimizing flow resistance. The Applicant submits that adding surface area or undulations inside small conduits ranging from 4 to 8 mm in size quickly creates flow passage resistance. By enabling single-lumen usage, the size of the device can be reduced substantially over multi-lumen devices. Plus, the available volume for heat exchange inside a small blood vessel is optimized with the maximum amount of heat exchange tubes and with those tubes being dynamic in operation.

**Reason 3 – 5:** The concept of a shuttle system was not suggested (#3) and the advantage of this feature was left unappreciated (#4). In fact if these advantages had been obvious, those skilled in the art likely would have implemented it by now (#5). Cooling catheter patents are well established concepts.

**Reason 6:** The principle of operation for the shuttle system is new. The cited references do not suggest the use of shuttle cooling, that is delivering and removing a working fluid in cyclical fashion to the heat exchange surface. Taheri, Figs. 1, 2 and 4 all show the working fluid is circulated. Dobak et al., Fig. 5, shows a cross sectional view of the catheter indicating the working fluid is circulated. In Pham et al., Figs. 1, 5, 7, and 9 all show the working fluid traveling in a circulatory path. Furthermore, the additional feature of creating motion in the heating exchange surfaces as a result of this shuttling is not recited in the above mentioned references.

**Reason 7:** The shuttle system solves a long felt and unsolved need to cool the blood inside small arteries (4-8 mm inner diameter). Again, to best of the Applicant's knowledge, a successful medical device that can cool ischemic organs through feeding arteries has not been accomplished.

**Reason 8 & 9:** Since the cited references do not introduce the concept of shuttling the working fluid, it is impossible to combine or "modify the catheter disclosed by Taheri" (Office Action, pg 4, 1<sup>st</sup> paragraph) to create the described shuttle system (#8). Shuttling fluid to and from the

inflatable designs as recited in the references would result in heat exchange surfaces expanding to possibly constrict the vessel and then collapsing as working fluid is withdrawn. In the collapsed position this design would not have substantial surface area to exchange heat, reducing catheter performance. Finally, the Applicant asserts that combining working fluid shuttling with a plurality of tubes and inflatable distal leads to an unobvious synergism not recited in the references (#9). The Applicant asserts that shuttling a working fluid into and out of a simple inflatable or flexible tube alone would not perform the heat transfer function well as explained above.

**Feature 6: a means to provide rotary motion to a plurality of heat exchange surfaces (grouped as “turbine system”) (Revised claims 38-42 formerly claim 12).**

**Reason 1:** The turbine system leads to new and unexpected results. The turbine system is able to combine substantial amounts of heat exchange surface area and blood side mixing into a compact profile so that flow resistance is minimized. In fact, the shape of the heat exchange surfaces can create a swirling motion to pull flow past the device.

**Reason 2:** The turbine system addresses an unrecognized or at least unappreciated problem of creating a blood flow restriction when attempting catheter heat transfer in small arteries. As the applicant has asserted, simply adding surface area will not enable users to meet a cooling catheter performance objective. This feature enables minimum use of surface area to maximize heat exchange while creating minimal flow resistance.

**Reason 3 – 5:** The concept of a turbine system was not suggested (#3) and the advantage of this feature was left unappreciated (#4). In fact if these advantages had been obvious, those skilled in the art likely would have implemented it by now (#5).

**Reason 6:** The principle of operation for the turbine system is new. The cited references do not suggest the use of a turbine system, that harnesses the hydraulic energy of the coolant (external to the body) to drive heat exchange surface motion and therefore augment heat transfer. Instead, only Taheri suggests using working fluid pressures for “preventing blood from clotting on the flexible portion.” (Column 4, paragraph 3).

**Reason 7:** The turbine system solves a long felt and unsolved need to cool the blood inside small arteries (4-8 mm inner diameter). Same reasons as given for features 3-5.

**Reason 8 & 9:** Since the cited references do not introduce the concept of a turbine system, it is impossible to combine or "modify the catheter disclosed by Taheri" (Office Action, pg 4, 1<sup>st</sup> paragraph) to create the described turbine system (#8). Missing elements would include the turbine proximal manifold and the sealed bearing connection. A plurality of tubes without the turbine system or vice versa would not lead to the synergism that enables heat exchange increases with minimal flow resistance (#9).

**Feature 7: a microporous membrane heat exchange surface with gas soluble working fluid flowing internally (grouped as "membrane system").** (Revised claims 18 formerly claim 13).

**Reason 1:** The membrane system leads to new and unexpected results. The membrane system is able to combine two functions onto one surface: heat transfer and mass transfer. As the Applicant has noted in the specification under "Detailed Description", changes in carbon dioxide concentrations can significantly increase blood perfusion to the regions of the brain. The membrane system may be used to alter this dissolve gas concentration and significantly alter blood perfusion levels, while simultaneously cooling the blood. The Applicant asserts that this new and unexpected result is not anticipated by the prior art.

**Reason 2:** The membrane system presents an unappreciated advantage of using single exchange surface to exchange both heat and mass. By exchange heat and mass with a single surface the blood flow resistance is minimized and as stated above alteration of blood perfusion levels may also be increased, a primary medical objective with ischemic organs.

**Reason 3 – 5:** The concept of a membrane system was not suggested (#3) and the advantage of this feature was left unappreciated (#4). Pham et al. suggests hollow fibers but only discusses their use in terms of heat transfer (column 6, paragraph three). Again, if these advantages had been obvious, those skilled in the art likely would have implemented it by now (#5).

**Reason 6: The principle of operation for the membrane system is new.** The cited references do not suggest the use of a membrane system that harnesses microporous materials to carry out simultaneous heat and mass transfer.

**Reason 7 & 8: Since the cited references do not introduce the membrane system concept it is impossible to combine or “modify the catheter disclosed by Taheri” (Office Action, pg 4, 1<sup>st</sup> paragraph) to create the described turbine system (#7).** Missing elements would include the membranes, the gas-soluble working fluid, and the external heat and mass exchanger (Applicant’s specification item 5, Fig. 5). Finally, the prior art references do not suggest that these features be combined in the manner suggested here (#8).

**Feature 8: a distal manifold for device alignment (grouped as “alignment system”) (Revised claim 43 formerly claim 8).**

**Reason 1: The alignment system leads to new and unexpected results.** The alignment system is able to be connected with existing commercially available distal protection filters to enable all the heat exchange surfaces of the device described in the invention to be in complete contact with flowing blood. A device which rest partially on the inner vessel wall will not be utilized in a full and complete sense. The Applicant asserts that when dealing with vessels that range in diameter from 4 to 10 mm, every square millimeter in exchange surface is critical.

**Reason 2: The principle of operation for the alignment system is new.** The cited references do not suggest the use of an alignment system that harnesses existing distal protection filter technology to maximize the possible amount of heat transfer.

**Reason 3 – 6: The concept of an alignment system was not suggested (#3) and the advantage of this feature was left unappreciated (#4).** Dobak et al. suggests using a guide wire or guide catheter to properly locate the device in the carotid artery (column 16, step 11), however Dobak et al. do not address the problem of device alignment for maximum heat transfer (#5). Again, if these advantages had been obvious, those skilled in the art likely would have implemented it by now (#6).

**Feature 9: distal orifices and controlled working fluid infusion (grouped as “infusion system”) (Revised claim 43 formerly claim 9).**

**Reason 1:** The infusion system leads to new and unexpected results. The infusion system enables rapid blood cooling through a concept called direct contact heat exchange. The control system is used to minimize the volume infused. Combining direct contact cooling – through infusion – with surface heat exchange leads to unexpected size catheter reductions, again this is imperative to maintain safe perfusion levels.

**Reason 2:** The principle of operation for the infusion system is new. The cited references suggest the use of infusion but not in the unobvious manner described in this invention. Referenced prior art such as Pham et al., Fig. 10, and Taheri, Fig. 3 both suggests infusion with the use of additional lumens to infuse. In addition, infusion of working fluid, the fluid used to do the cooling is not suggested to aid the heat transfer process. These additional lumens again add additional size, further increasing blood flow resistance.

**Reason 3:** References teach away from the infusion system.

Dobak et al., column 2, paragraph four, teaches against infusion of working fluid. Dobak et al sites these drawbacks: “volume accumulation, cost, and inconvenience of maintaining perfusate and lack of effectiveness due to temperature dilution from the blood.” The infusion system addresses many of these drawbacks. The combined surface heat exchange and direct contact heat exchange reduce the need for large volume introductions. Working fluid infusion is automated through the control system (Fig. 1, item 11). The Applicant asserts that temperature dilution is not a problem as a direct contact heat exchange system is a well-established technology in the many engineering applications. In fact, the Applicant has calculated that for every millimeter per minute of working fluid introduced, about 2.3 watts of cooling can be achieved if the working fluid is introduced at 4 degrees Celsius.

**Reason 4:** Direct contact heat exchange through controlled working fluid infusion is unappreciated advantage. Up to know, those skill in the art have not appreciated the advantages of using direct contact heat exchange in combination with surface heat exchange as described in

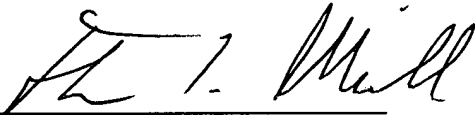
the infusion system. The Applicant asserts that concern from "volume accumulation" and control have led to this combination not being suggested in the prior art.

### CONCLUSION

Applicant respectfully submits that all stated grounds for objection and rejection have been properly traversed, accommodated, and rendered moot. Applicant submits that all revised claims are in condition for allowance. The examiner is invited to telephone the undersigned Applicant if a discussion or interview might be useful to place the application in better condition for allowance.

The Applicant sincerely appreciates the Examiner's willingness to provide guidance in this office action response.

Sincerely,

A handwritten signature in black ink, appearing to read "T. L. Merrill", is written over a horizontal line.

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